REVIEW

New methods for improved evaluation of patients with suspected acute coronary syndrome in the emergency department

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This paper aims to identify and review new and unproven emergency department (ED) methods for improved evaluation in cases of suspected acute coronary syndrome (ACS). Systematic news coverage through PubMed from 2000 to 2006 identified papers on new methods for ED assessment of patients with suspected ACS. Articles found described decision support models, new ECG methods, new biomarkers and point-of-care testing, cardiac imaging, immediate exercise tests and the chest pain unit concept. None of these new methods is likely to be the perfect solution, and the best strategy today is therefore a combination of modern methods, where the optimal protocol depends on local resources and expertise. With a suitable combination of new methods, it is likely that more patients can be managed as outpatients, that length of stay can be shortened for those admitted, and that some patients with ACS can get earlier treatment.

Coronary heart disease is the single largest killer in Europe. If European figures are comparable to American,[1] at least 10 million Europeans present to the emergency department (ED) each year for symptoms compatible with acute myocardial infarction (AMI) or unstable angina—that is, acute coronary syndrome (ACS). For the patients in whom ACS is detected, treatment has improved tremendously over the last two decades, and we now intervene in the ischaemic process and effectively prevent morbidity and mortality. In contrast, during the same period the ED evaluation of patients with suspected ACS has been almost unchanged, and the quality must now be considered to be unsatisfactory. Some seven out of 10 patients admitted from the ED with a suspicion of ACS prove not to have it,[2 3] and many of these patients are observed at a high level of care.[2] At the same time, many ACS patients are identified only after in-hospital observation, with a resulting delay in treatment and impaired prognosis. As many as 2–5% of the patients with ACS are even erroneously sent home from the ED.[4] There is thus a great need for new evaluation methods that can increase quality of care for the many patients, and allow limited health care resources to be focused on patients with true ACS, where rapid intervention clearly improves the prognosis.

A number of new methods are available for improving the ED evaluation and management of patients with suspected ACS, and this review aims to summarise them, and to look at their advantages and disadvantages.

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LITERATURE SEARCH

To address the aim, the literature was searched weekly during 2005 and 2006 through ''My NCBI'' at PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB = pubmed) using the criteria ''Angina, Unstable/diagnosis''[MeSH] OR ''Myocardial Infarction/diagnosis''[MeSH]. A total of 2202 papers were identified. An additional PubMed search for articles in English since 2000 using ''Myocardial Ischemia/diagnosis''[MeSH] AND ''Emergency Service, Hospital''[MeSH] yielded 391 papers. Papers subjectively deemed relevant were retrieved, and the reference lists were reviewed for additional articles of interest. In general, abstracts were disregarded.

NEW METHODS FOR EMERGENCY DEPARTMENT EVALUATION OF PATIENTS WITH SUSPECTED ACUTE CORONARY SYNDROME

Decision support models

In principle, ED evaluation can be improved either by increasing the information on which management decisions are based (that is, adding new diagnostic methods), or by making better use of the information already available. The latter is potentially inexpensive, and often involves the use of a clinical decision support system. Such systems may raise the quality of care in the ED by preventing errors, by increasing adherence to guidelines and by introducing an evidence based approach to patient management. Decision support systems for suspected ACS are usually based on electrocardiographic (ECG) and clinical variables and can be a simple set of forms with management directions, or include a computerised model based on logistic regression or artificial neural networks.

A large number of decision support models have been created.[5–12] Some predict the risk of complications, but the majority of the published models have been focused on diagnosing AMI. With the current ACS paradigm, however, models that

Abbreviations: AMI, acute myocardial infarction; ACS, acute coronary syndrome; BNP, B-type natriuretic peptide; CPU, chest pain unit; CRP, C reactive protein; ECG, electrocardiogram; ED, emergency department; MDCT, multidetector computed tomography; MPI, myocardial perfusion imaging; MRI, magnetic resonance imaging

predict AMI are often less useful in routine ED care, where the likelihood of ACS (rather than AMI) is normally decisive for admission or discharge, and for immediate treatment. Also, many of the published models need substantial input from the ED personnel,[5 6] and hence are not ideal for use in the standard care at a busy ED. Few prediction models[11 12] identify patients suitable for immediate reperfusion treatment. Only two models[7 10] have been both easy to use and predictive of ACS. The validated one, the ACI-TIPI score, decreased unnecessary admissions somewhat in non-ACS patients in 10 larger US hospitals.[7] In small US hospitals, however, using the score did not improve diagnostic accuracy or change triage.[13] It is important to note that clinical prediction rules are specific and not immediately transferable, and therefore should be validated for each patient population.

One of the most useful decision support models for ED use so far seems to be that of Goldman *et al*[8] that predicts cardiac complications within 72 h, and suggests the level of in-hospital care. The model deals with clinically important events, recommends specific action and, most importantly, is well validated.[14] The model postulates that only patients with ECG evidence of ischaemia and at least two of three ''urgent factors'' (rales above both lung bases, systolic blood pressure $<$100 mm Hg and specified symptoms of unstable ischaemic heart disease) need admission to a coronary care unit. In a prospective impact trial,[14] use of the model decreased the improper triage of low risk patients to higher levels of care. It is noteworthy that the Goldman model does not identify patients suitable for ED discharge. For optimal management decision support, the Goldman model could perhaps be combined with a new diagnostic method or a decision support model for ACS detection. A patient with a very low risk of ACS and of cardiac complications could probably be discharged home from the ED, for outpatient follow up.

At the moment, many of the published decision support models thus lack clinical validation, and this is of course imperative before implementation in routine care. Validation trials should preferably have a multicentre design and analyse not only healthcare process measures, but also the important patient outcomes such as morbidity and/or mortality.

New ECG methods

Standard ECG recording is rapid, inexpensive and universally available. Several new ECG methods have been presented, but none seems yet ready to be taken up in standard care.

Body surface mapping with up to 80 leads on the torso is a method to expand the ''visual field'' of the standard ECG. The method has a higher sensitivity for detecting major AMI than the standard ECG,[15] but an added value for detection of ACS without significant myocardial necrosis has not been shown. A danger is that a low specificity for AMI detection compared to the standard ECG may lead to an overdiagnosing of AMI.[15]

Differences in QT intervals among the ECG leads (QT dispersion) probably represent repolarisation inhomogeneity and have been suggested to be valuable for the emergency diagnosis of AMI.[16] There are no data regarding its usefulness for diagnosing unstable angina. The value of QT dispersion in the ED is probably limited because of a relatively large normal variation.[17]

A method with potential to detect acute myocardial ischaemia[18] in the ED is analysis of high frequency components in the QRS complex (150–250 Hz; HF-QRS). HF-QRS seems better than standard ST segment deviation at detecting ischaemia induced by balloon angioplasty,[19] but it remains to be elucidated whether HF-QRS can help identify ACS or AMI in ED patients. Hardware and software for HF-QRS recording and analysis in the ED are now available.

Point-of-care testing and new biomarkers

Rapid analyses of blood samples in the ED, point-of-care testing, have become common and may provide results within 15 min, compared to perhaps 1–1.5 h from the core lab at the clinical chemistry department. This may allow more efficient patient turnaround,[20] and offers the advantage of owning the analysis in the ED. The advantages must, however, be weighed against the cost and the need for personnel. In addition, the first ED results for markers of myocardial necrosis (for example, troponin or creatine kinase MB) should often not be decisive for patient management, since levels are not pathological in unstable angina, and the sensitivity at presentation for AMI is below 50%.[21] As described below, markers to detect ACS without myocardial necrosis (unstable angina) are not yet ready for clinical use.

If several markers are combined, perhaps with a mathematical index to integrate the results of the different markers, performance is improved.[22] Using multiple markers, it may be possible to attain a sensitivity and specificity over 90% for AMI at ED presentation,[23] and safe exclusion of AMI in 90 min.[24] However, after the publication of new thresholds for AMI diagnosis by the European Society of Cardiology and the American College of Cardiology,[25] many studies can no longer be used as a basis for practice guidelines. Indeed, the American College of Emergency Physicians states that there is now insufficient evidence for recommendations regarding the use of serum markers to exclude AMI[26] in the ED. A great need for new studies has emerged.

In a continuous search for the perfect biomarker, a multitude of new analyses have been proposed for diagnosis and risk prediction in patients with possible ACS, and several reviews are available.[27–30] New markers of necrosis and ischaemia include heart-type fatty acid binding protein, ischaemia modified albumin, and B-type natriuretic peptide (BNP). In ACS patients, high BNP values indicate an increased risk for heart failure or death,[31] but whether BNP can be used to identify patients with ACS in the ED needs further investigation.[32] Proposed markers of inflammation and plaque instability include myeloperoxidase, soluble CD40 ligand, and C reactive protein (CRP). CRP is valuable for determining long term prognosis,[30] but its usefulness in the ED evaluation for suspected ACS remains to be shown. Several markers of activated haemostasis have been studied—for example, soluble fibrin—but are for the moment not useful in the routine clinical diagnosis of ACS.[27]

Although several of the new markers are very promising, in many studies comparisons have been made only with troponin at high (and outdated) cut-off levels,[29] which means that data are lacking regarding the detection of small infarctions or unstable angina. In addition, prospective studies are scarce and many analyses are not yet available as approved commercial kits. Further research is clearly needed and will hopefully show which markers can be applied in routine care. It would be especially rewarding to have high quality biomarkers of myocardial ischaemia, since this would allow physicians to interfere earlier in the ischaemic process and to limit or prevent AMI.

New cardiac imaging methods

Another alternative is to introduce new cardiac imaging methods in the ED.[33] These methods are of course not available at all hospitals, but are interesting for large centres with high patient volumes. It should be noted that many clinical imaging studies were performed before the current definition of AMI,[25] and that caution should be exercised when applying the results in routine care.

Echocardiography with the new commercially available contrast agents can assess myocardial perfusion and wall motion abnormalities at the bedside, and in real time.[34–36] Additional advantages are the portability and that it can

diagnose other causes of chest pain such as aortic dissection. Downsides are the dependence on operator skill and suitable patient anatomy, with low image quality in, for example, obese patients. With highly skilled personnel, however, a sensitivity of 100% and specificity of 93% for ACS detection have been reported in ED chest pain patients.[37]

Rest nuclear myocardial perfusion imaging (MPI)[38] has been shown to be of true value in routine care,[39] primarily because of a negative predictive value for ACS of 99–100% in patients with ongoing or recently abated chest pain and a normal ECG. In these ED patients, MPI is jointly recommended by the American College of Cardiology/American Heart Association/American Society of Nuclear Cardiology,[40] and US studies suggest that this practice is cost effective.[41] MPI is well suited for remote interpretation using telemedicine systems. Because of the imaging of perfusion, there is also a potential for earlier detection of ACS, but published positive predictive values are low, and the clinical value of the method for this purpose remains to be shown. Timing of the isotope injection seems crucial,[38] and an injection later than 2 h after symptoms decreases sensitivity and the negative predictive value. The radiation is a disadvantage. Only one study[42] has analysed MPI performance with newer definitions of AMI, and further research in this area is needed.

Multidetector computed tomographic scanning (MDCT)[43 44] is a promising modality that, like echocardiography, identifies several causes of chest pain, that is very rapid (single breath-hold) and that, like MPI, does not need an on-site physician. Disadvantages are the need for a low patient heart rate because of the temporal resolution, the need for an intravenous contrast agent, the radiation, and the difficulty in interpreting images from patients with coronary stents or previous bypass surgery. Despite the fact that MDCT detects coronary artery stenosis and plaque and not ischaemia, it probably has a very high negative predictive value for ACS, and may reduce unnecessary admissions for suspected ACS.[45]

Magnetic resonance imaging (MRI) has not been extensively studied, but is theoretically attractive for comprehensive evaluation of ED chest pain patients. In a study by Kwong *et al*,[46] MRI within 12 h of admission had a sensitivity of 84% and specificity of 85% for ACS detection, and added diagnostic value over clinical parameters. Weaknesses with current MRI technology are long scan times, that a potentially unstable patient is relatively isolated in the scanner, and that the patient cannot have certain metal prostheses. Technology development and further studies will most certainly follow.

Immediate exercise test

Immediate exercise tests in the ED for low risk patients seem feasible, inexpensive, safe and accurate for determining those who can be discharged for further outpatient evaluation,[47 48] but is probably not as widely used as it could. The fear of mistakenly testing a patient with ACS is likely large, but may be exaggerated in the appropriately selected population.[48] Contraindications to exercise testing in this situation include ischaemic ECG changes, aortic stenosis, obvious unstable angina, uncompensated heart failure, dysrhythmias and uncontrolled hypertension.

The chest pain unit concept

The comprehensive solution, but one that requires ED and/or hospital reorganisation, is to establish a chest pain unit (CPU) with dedicated beds and personnel. In the USA, a significant fraction of all hospitals now have a CPU,[49] connected either to the ED or the coronary care unit. The interest in Europe is growing,[50–52] but slowly. In the CPU, low risk patients with unclear symptoms and a non-ischaemic ECG are subjected to an accelerated diagnostic protocol, often during 6–12 h. Depending on local resources and expertise, the CPU protocols include telemetry or ST segment monitoring, repeated blood samples, echocardiography and provocative testing, and the CPU can thus be regarded as a means of applying available diagnostic methods in a more effective way. Common exclusion criteria for CPU care are dysrhythmia, decompensated heart failure, and inability to perform an exercise test.

Is establishing a CPU worth it? Probably yes, but the answer depends on patient volume and how the unit is implemented. Several studies describe the advantage of a CPU (for example, see Blomkalns and Gibler[1]) and randomised controlled trials have been presented,[53–56] albeit mostly from the USA, but no study has compared CPUs with traditional ED evaluation supplemented by special investigations such as echocardiography or MPI. Taken together, however, the available data indicate that CPUs can increase cost effectiveness, decrease length of stay for patients without ACS, allow faster diagnosis and intervention in patients with ACS, at a quality of care (morbidity and mortality) at least as good as traditional care.[57] Cost savings have been reported per evaluated patient,[56] but not yet at the hospital level.

It is worth stressing that the CPU concept is a response to an unsatisfactory diagnostic quality in the ED. It may well be that better diagnostic methods or strategies in the ED will decrease or even eliminate the benefits of establishing dedicated CPUs.[58] For the time being, a strictly implemented accelerated diagnostic protocol without dedicated beds or personnel is an attractive solution for hospitals with smaller patient volumes, or limited ability to reorganise.

CONCLUSION

The ED evaluation quality in cases of suspected ACS is clearly suboptimal, and the number of patients affected very large. This lack of quality leads to over-admission of patients to in-hospital care, to delayed diagnosis and to erroneous discharge home. Many new methods for improved ED evaluation have been presented and may be implemented, and the development seems particularly promising in the fields of acute imaging and blood analyses. At this time, however, there seems to be no one method to solve all the problems at hand.

To counter over-admission and erroneous discharge, we need cost effective methods with proven high sensitivity and negative predictive value for ACS (and not only AMI). MPI, and perhaps also MDCT, are able to rule out ACS in low risk ED patients but are not available at all hospitals. Immediate exercise tests may be an alternative. Where available, MPI together with Goldman's model for prediction of cardiac complications could be a combined tool to identify patients suitable for ED discharge, and outpatient follow up. To diagnose ACS earlier, and hence be able to start treatment earlier, the primary need is reliable methods to rapidly detect myocardial ischaemia. MPI is theoretically attractive in this respect, but its positive predictive value is probably too low in the ED patient population. New blood samples or ECG methods can be the solution, but remain to be tested in the real clinical situation.

The best overall strategy today seems to be a combination of methods—for example, multiple biomarkers together with cardiac imaging and a decision support model for patient disposition. For the time being, the optimal evaluation protocol thus depends on local resources and expertise, and is probably somewhat different for each hospital. Whatever the strategy, it seems clear that the structured and evidence based use of the available methods, with or without a formal chest pain unit, is essential in order to improve quality of care for all patients with suspected ACS. This will also allow scarce healthcare resources to be focused on patients with true ACS, where our ability to decrease morbidity and mortality is well documented.

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